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Stereoselective Formation of Eight-Membered Rings by Radical Cyclization of Silylenedioxy-Tethered Bis-methacrylate Derivatives

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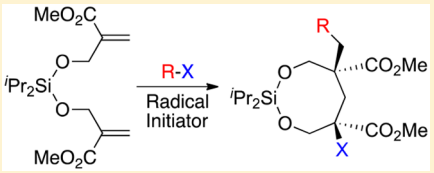
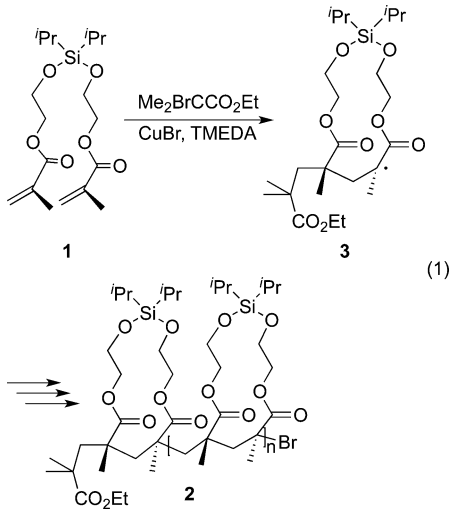
Supporting Information

ABSTRACT: Radical-initiated addition of CCl_4, Cl_3CBr, PhSH, and $(TMS)_3SiH$ to (bisisopropyl)silylenedioxy-tethered bis-methacrylate derivatives gives the corresponding eight-membered ring cyclic adducts stereoselectively. Hydrolysis of halo-substituted cyclic adducts with HCl in methanol affords the corresponding valerolactones, and the stereochemistry was determined by the X-ray crystallography on a dibromobenzoate derivative. DFT calculation on the eight-membered radical intermediate offers a plausible rationale for the stereoselectivity of the reaction.



Radical cyclizations have been demonstrated to constitute a powerful arsenal for the construction of cyclic products of a wide range of structural varieties.[1−7] The reaction is particularly useful for the synthesis of five- and six-membered rings with well-controlled stereoselectivity.[1] The applications of radical cyclizations leading to medium-sized rings have also been explored.[2−6]

Like many other cyclization reactions where germinal substituents on the tether may facilitate the reactions, known as the Thorpe−Ingold effect,[7] similar behavior has been observed in radical cyclization.[8] Silicon tethers has also been extensively used in cyclization reactions,[9,10] particularly in radical cyclization,[5a,11] and the silicon tethers can readily be removed afterward. This strategy offers versatile entries for the selective synthesis of products with fascinating structural complexities. Since carbon−silicon bonds are longer than those of carbon−carbon bonds and the rotation barriers for carbon−silicon bonds are much smaller than those of carbon−carbon bonds,[12] little attention has been paid to the Thorpe−Ingold effect in organosilicon derivatives.[13−15] We recently found that the presence of bulky isopropyl substituents on silicon in silylene-space divinylarene copolymers may exert the Thorpe−Ingold effect, which can bring two adjacent chromophores to closer proximity so that the photophysical properties of these copolymers may be perturbed.[14] In addition, the ATRP-induced cyclopolymerization of bis-methacrylate **1** tethered by a substituted silylene moiety has been shown to be somewhat *r*-selective for the formation of polymer **2** containing 14-membered cyclic monomeric units (eq 1).[15,16] Under these reaction conditions, it would be difficult to stop at cyclization intermediate **3**. It is known that the radical promoted Kharasch addition and related reactions onto acrylate derivatives to give the corresponding adducts.[16b] We envisioned that a careful control of reaction conditions may selectively cyclize a bis-methacrylate derivative to give the corresponding cyclic product. In order to test the generality of this cyclization, we now wish to report the stereoselective formation of eight-membered rings by radical cyclization of silylenedioxy-tethered bis-methacrylate **4**.



Bis-methacrylate **4** was obtained by silylation of **6**[17] with $^iPr_2SiCl_2$. Treatment of **4** with $BrCCl_3$ (8 equiv) in the presence of AIBN (0.13 equiv) and Cu(TPMA)Cl (**7**, 0.2 mol %)[18] in toluene at 60 °C for 24 h afforded **8a** as the single diastereomer in 58% yield (eq 2).[19,20] Hydrolysis of **8a** with methanolic HCl gave valerolactone **10** in 82% yield. The X-ray structure of the corresponding dibromobenzoate **12** is shown in Figure 1.

The relative stereochemistries of the asymmetric centers in **8a** were thus assigned. Similarly, reaction of **4** with CCl_4 under the same conditions gave 45% yield of a mixture of **8b** and **9b** in a ratio of 97 to 3. Removal of the silylene tether from **8b** furnished

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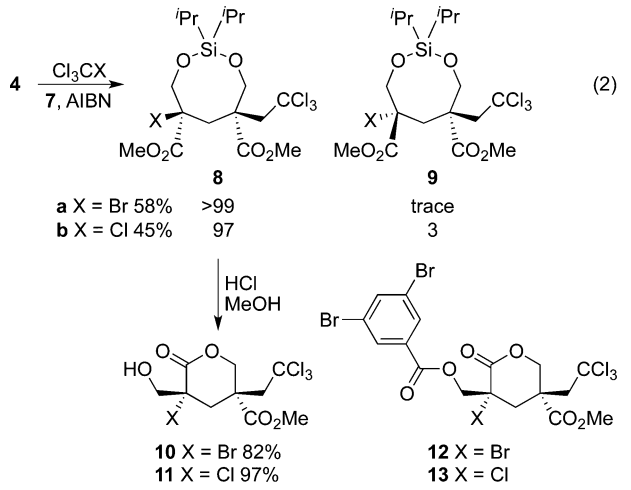


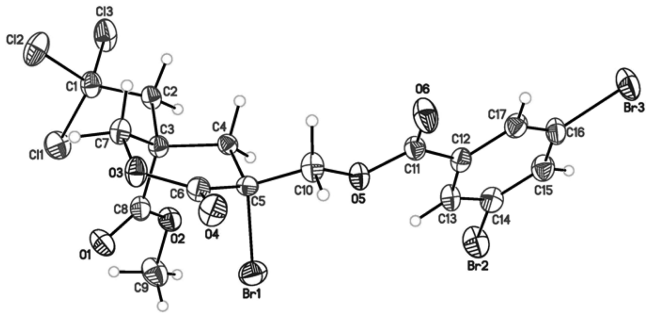
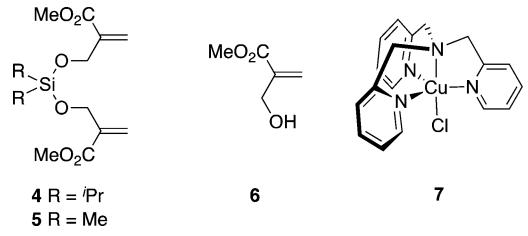


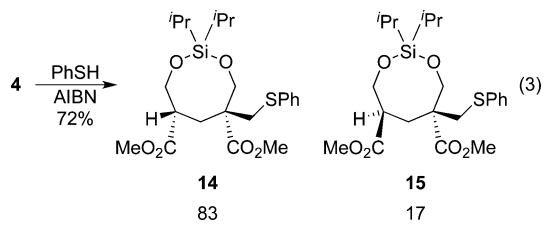
Figure 1. ORTEP structure of **12** (50%).



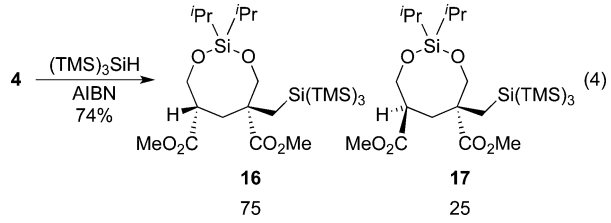
11 in 97% yield, which was also converted into dibromobenzoate **13** in 79% yield.[19]

The high diastereoselectivity of this radical cyclization for the formation of an eight-membered ring is interesting. Presumably, the halogen atom transfer from the copper catalyst[18] takes place preferentially from the less hindered pseudoequatorial site, rendering the stereoselective formation of adduct **8a**.

Reaction of **4** with PhSH in the presence of AIBN (6 mol %) in refluxing ^{t}BuOH[21,22] for 12 h gave 72% yield of the corresponding adducts **14** and **15** in a ratio of 83 to 17.[19,20] The stereochemical assignments were based on ROESY spectra.[19]



In a similar manner, $(TMS)_3SiH$[23] also added to **4** to afford **16** and **17** (75:25) in 74% yield. It is worth mentioning that the diastereoselectivities of these reactions were similar to those of halogen abstractions described above, giving *cis*-dicarboxylates as the major products.



It seems likely that the bulky isopropyl groups in **4** may exert the Thorpe−Ingold effect to favor the *syn* conformation, resulting in stereoselective radical cyclization as depicted above. The incorporation of smaller methyl substituents on silicon may behave differently. Thus, reaction of **5** with PhSH under the same conditions in ^{t}BuOH as described above gave a mixture of **18** and **19** (60:40) in addition to other minor impurities.[24] Apparently, the less sterically hindered methyl substituents on silicon offer a less hindered environment for atom-transfer process. The reaction is less stereoselective than those with isopropyl substituents on silicon.

The stereoselectivity of the radical promoted cyclization for medium-sized rings, in general, is not satisfactory without external assistance. Li and co-workers have found that chelation by Lewis acids may improve the situation significantly.[4j] In this study, the presence of bulky isopropyl substituents apparently directs the atom-transfer process selectively. Preliminary DFT calculations on the radical intermediate **20** with the Gaussian 09 program[25] using the B3LYP hybrid function[26] and the 6-311G +(d,p) basis sets for all the elements suggest that atom-transfer reaction may preferentially take place from the pseudoequatorial site, rendering the formation of eight-membered rings stereoselectively (Figure 2).

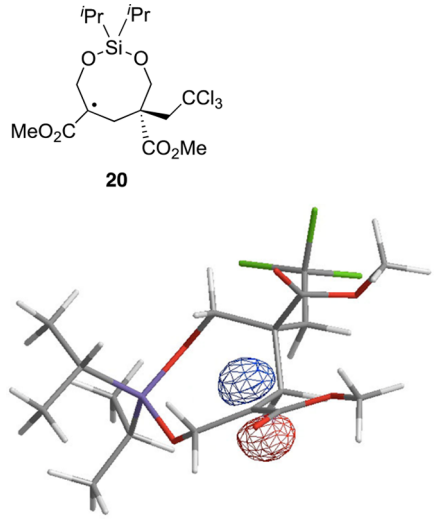


Figure 2. DFT calculation of radical intermediate **20**.

In summary, we have demonstrated a useful radical cyclization of a bis-methacrylate derivative tethered by a (bisisopropyl)-silylenedioxy linker giving the corresponding eight-membered adducts stereoselectively. Like other cyclization reactions for the formation of eight-membered rings,[4] selective 8-*endo* cyclization was observed in all cases in this study. The isopropyl substituents

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may not only exert the Thorpe−Ingold effect for the cyclization process but also make the atom-transfer process stereoselective.

EXPERIMENTAL SECTION

General Information. High-resolution mass spectroscopy was obtained by using the FAB method with a magnetic sector analyzer, or the ESI method with a TOF analyzer.

Bis(2-methoxycarbonyl)allyl Diisopropylsilyl Ether (4). To a solution of **6**[16] (5.00 g, 43.0 mmol) and imidazole (4.39 g, 64.5 mmol) in DCM (150 mL) was added dropwise dichlorodiisopropylsilane (4.11 g, 22.2 mmol) cooled in an ice bath, and the reaction mixture was stirred overnight at rt. Then, the precipitate was filtered and the filtrate was washed 3 times with brine. After dried ($MgSO_4$), the solvent was removed in vacuo, and the residue was chromatographed on silica gel (hexane/EtOAc = 10/1) to give **4** as a colorless oil (5.4 g, 73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ1.05−1.09 (m, 14 H), 3.75 (s, 6 H), 4.49 (s, 4 H), 5.96 (d, J = 2.4 Hz, 2 H), 6.27 (d, J = 2.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.0, 17.2, 51.6, 61.1, 123.9, 139.1, 166.1. IR (KBr) ν 2997, 2951, 2869, 1727, 1641, 1462, 1392, 1310, 1275, 1096 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{28}O_6SiNa$: 367.1547 ([M + Na]$^+$), found: 367.1552.

Bis(2-methoxycarbonyl)allyl Dimethylsilyl Ether (5). To a solution of **6** (4.4 g, 38.0 mmol) and TEA (5.7 g, 57.0 mmol) in THF (50 mL) was added dropwise dichlorodimethylsilane (2.46 g, 19.0 mmol) cooled in an ice bath, and the mixture was stirred overnight at rt. The precipitate was then filtered, and the filtrate was washed 3 times with brine. After dried ($MgSO_4$), the solvent was removed in vacuo, and the residue was chromatographed on silica gel (hexane/EtOAc = 10/1, 0.1% TEA added) to give **5** as a colorless oil (2.46 g, 45%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.19 (s, 6 H), 3.75 (s, 6 H), 4.43 (s, 4 H), 5.89 (d, J = 1.7 Hz, 2 H), 6.27 (d, J = 1.7 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −3.4, 51.7, 60.9, 124.4, 138.9, 166.2. IR (KBr) ν 3001, 2955, 2908, 2873, 1723, 1642, 1439, 1310, 1092, 804 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{20}O_6SiNa$: 311.0927 ([M + Na]$^+$), found: 311.0919.

4,6-*cis*-Bis(methoxycarbonyl)-4-(2,2,2-trichloroethyl)-6-bromo-1,1-diisopropyl-1-sila-2,8-dioxacyclooctane (8a). To a solution of **4** (742 mg, 2.15 mmol), AIBN (45 mg, 0.27 mmol), bromotrichloromethane (3.42 g, 17.3 mmol) in toluene (7 mL) was added at rt the catalyst solution (70 μL, 0.05 M), prepared by dissolving CuCl (0.0990 g, 1.00 mmol) and tris(2-pyridylmethyl)amine (TPMA, 0.290 g, 1.00 mmol) in methanol (20.0 mL) in a glovebox, and the mixture was stirred at 60 °C for 24 h. The solvent was then evaporated in vacuo, and the residue was purified by chromatography on silica gel (hexane/EtOAc = 10/1) to afford **8a** (673 mg, 58%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07−1.16 (m, 13 H), 1.26 (hept, J = 7.5 Hz, 1 H), 2.73 (d, J = 14.5 Hz, 1 H), 2.78 (d, J = 14.5 Hz, 1 H), 3.14 (d, J = 15.2 Hz, 1 H), 3.53 (d, J = 15.2 Hz, 1 H), 3.69 (s, 3H), 3.78 (s, 3 H), 4.31 (d, J = 13.2 Hz, 1 H), 4.35 (d, J = 13.2 Hz, 1 H), 4.36 (d, J = 14.2 Hz, 1 H), 4.60 (d, J = 14.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 11.8, 17.3, 17.4, 17.5, 40.6, 52.3, 53.0, 57.8, 60.2, 64.3, 67.8, 94.3, 95.9, 169.0, 172.0. IR (KBr) ν 2954, 2869, 1746, 1465, 1438, 1287, 1252, 1083, 886, 778 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{28}{}^{79}Br^{35}Cl_3O_6SiNa$: 562.9802 ([M + Na]$^+$), found: 562.9804.

4,6-*cis*- and 4,6-*trans*-Bis(methoxycarbonyl)-4-(2,2,2-trichloroethyl)-6-chloro-1,1-diisopropyl-1-sila-2,8-dioxacyclooctane (8b) and (9b). To a solution of **4** (1.81 g, 5.30 mmol), AIBN (87 mg, 0.53 mmol), carbon tetrachloride (6.54 g, 42.5 mmol) in toluene (12 mL) was at rt added the catalyst solution (200 μL, 0.05 M) prepared according to a procedure described above, and the mixture was stirred at 60 °C for 24 h. The precipitate was filtered, and the filtrate was evaporated in vacuo to give the residue, which was chromatographed on silica gel (hexane/EtOAc = 10/1) to get a mixture of **8b** and **9b** (97:3), and a further purification was proceeded by chromatography on silica gel (hexane/EtOAc = 15/1) to afford **8b** (1.16 g, 44%) and **9b** (33 mg, 1%). Analytical pure samples were obtained by preparative HPLC (hexane/THF = 20/1). **8b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07−1.10 (m, 13 H), 1.23 (hept, J = 7.5 Hz, 1 H), 2.58 (ABq, J = 14.9 Hz, 2 H), 3.14 (d, J = 15.3 Hz, 1 H), 3.43 (d, J = 15.3 Hz, 1 H), 3.65 (s, 3 H), 3.75 (s, 3 H), 4.19 (d, J = 13.7 Hz, 1 H), 4.28 (d, J = 13.0 Hz, 1 H), 4.35 (d, J = 13.0 Hz, 1 H), 4.62 (d, J = 13.7 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.2, 11.5, 17.1, 17.2, 17.3, 40.2, 52.1, 52.2, 53.1, 58.1, 60.2, 67.5, 71.0, 96.0, 169.1, 172.2. IR (KBr) ν 2951, 2868, 1746, 1439, 1289, 1249, 1083, 885, 815, 750 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{29}{}^{35}Cl_4O_6Si$: 497.0488 ([M + H]$^+$), found: 497.0482. **9b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98−1.01 (m, 7 H), 1.07 (d, J = 7.5 Hz, 6 H), 1.22 (hept, J = 7.5 Hz, 1 H), 2.50 (d, J = 15.7 Hz, 1 H), 2.57 (d, J = 15.7 Hz, 1 H), 3.13 (d, J = 15.1 Hz, 1 H), 3.43 (d, J = 15.1 Hz, 1 H), 3.69 (s, 3 H), 3.80 (s, 3 H), 4.22 (d, J = 12.2 Hz, 1 H), 4.40 (d, J = 12.2 Hz, 1 H), 4.48 (d, J = 13.4 Hz, 1 H), 4.57 (d, J = 13.4 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.1, 11.5, 17.0, 17.1, 17.2, 17.3, 37.8, 50.6, 52.2, 53.6, 58.7, 59.4, 66.8, 67.2, 95.9, 170.1, 172.8. IR (KBr) ν 2954, 2868, 1744, 1462, 1438, 1238, 1127, 1082, 886, 817 cm^{-1}; HRMS (FAB) calcd. for $C_{17}H_{29}{}^{35}Cl_4O_6Si$: 497.0488 ([M + H]$^+$), found: 497.0493.

2*R*-Bromo-2-hydroxymethyl-4*R*-(2,2,2-trichloroethyl)-2-methoxycarbonylvalerolactone and Its Enantiomer (10). To **8a** (347 mg, 0.64 mmol) was added 0.1 M HCl in MeOH (30 mL), and the mixture was refluxed for 3 h. After cooling to rt, the solvent was removed in vacuo, and the residue was purified by recrystallization with hexane/EtOAc to afford the product **10** (209 mg, 82%): mp 154−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (m, 1 H), 2.90 (d, J = 16.5 Hz, 1 H), 2.97 (d, J = 16.5 Hz, 1 H), 3.16 (d, J = 15.5 Hz, 1 H), 3.47 (d, J = 15.5 Hz, 1 H), 3.64 (dd, J = 9.0, 11.7 Hz, 1 H), 3.83 (s, 3 H), 4.32 (dd, J = 6.1, 11.7 Hz, 1 H), 4.83 (d, J = 12.4 Hz, 1 H), 5.24 (d, J = 12.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.7, 44.8, 51.2, 53.2, 58.6, 67.7, 68.6, 94.8, 167.5, 171.4; IR (KBr) ν 3417, 2981, 2954, 2939, 1735, 1469, 1449, 1380, 1306, 890 cm^{-1}; HRMS (FAB) calcd. for $C_{10}H_{13}{}^{79}Br^{35}Cl_3O_5$: 396.9012 ([M + H]$^+$), found: 396.9011.

2*R*-Chloro-2-hydroxymethyl-4*S*-(2,2,2-trichloroethyl)-2-methoxycarbonylvalerolactone and Its Enantiomer (11). To **8b** (377 mg, 0.76 mmol) was added 0.1 M HCl in MeOH (30 mL), and the mixture was refluxed for 3 h. After cooling to rt, the solvent was removed in vacuo, and the residue was purified by recrystallization with hexane/EtOAc to afford the product **11** (259 mg, 97%): mp 148−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (m, 1H), 2.80 (d, J = 16.1 Hz, 1 H), 2.85 (d, J = 16.1 Hz, 1 H), 3.16 (d, J = 15.5 Hz, 1 H), 3.50 (d, J = 15.5 Hz, 1 H), 3.58 (dd, J = 8.0, 11.5 Hz, 1 H), 3.81 (s, 3 H), 4.21 (dd, J = 5.2, 11.5 Hz, 1 H), 4.75 (d, J = 12.4 Hz, 1 H), 5.19 (d, J = 12.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.3, 44.6, 53.2, 58.9, 60.2, 67.3, 69.3, 94.9, 167.3, 171.6; IR (KBr) ν 3413, 2981, 2954, 2885, 1739, 1445, 1388, 1129, 1017, 893 cm^{-1}; HRMS (FAB) calcd. for $C_{10}H_{13}{}^{35}Cl_4O_5$: 352.9517 ([M + H]$^+$), found: 352.9527.

3,5-Dibromobenzoate of 2*R*-Bromo-2-hydroxymethyl-4*R*-(2,2,2-trichloroethyl)-2-methoxycarbonylvalerolactone and Its Enantiomer (12). To a solution of 3,5-dibromobenzoic acid (310 mg, 1.1 mmol) in DCM (10 mL) at 0 °C was added oxalyl chloride (0.2 mL, 2.3 mmol) and DMF (1 drop). The mixture was gradually warmed to rt and stirred for 1 h. The solvent was removed in vacuo to give the corresponding acid chloride, which was used for the next reaction without further purification. To a mixture of **10** (291 mg, 0.73 mmol), TEA (0.21 mL, 1.51 mmol), and a trace amount of DMAP in DCM (10 mL) was added the freshly prepared acid chloride (1.1 mmol) described above in DCM (10 mL) at 0 °C. The mixture was stirred at rt for 12 h. Saturated $NaHCO_3$ aqueous solution was added, and the solution was washed with brine, and then dried over $MgSO_4$. The reaction mixture was concentrated in vacuo, and the residue was recrystallized by hexane/EtOAc to give **12** (420 mg, 87%): mp 148−150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81 (d, J = 16.5 Hz, 1 H), 3.21 (d, J = 16.5 Hz, 1 H), 3.25 (d, J = 15.5 Hz, 1 H), 3.46 (d, J = 15.5 Hz, 1 H), 3.85 (s, 3 H), 4.68 (d, J = 11.4 Hz 1 H), 4.77 (d, J = 12.4 Hz, 1 H), 4.96 (d, J = 11.4 Hz, 1 H), 5.23 (d, J = 12.4 Hz, 1 H), 7.89 (t, J = 1.8 Hz, 1 H), 8.04 (d, J = 1.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.2, 44.7, 48.4, 53.4, 59.0, 68.4, 69.3, 94.7, 123.3, 131.4, 132.0, 139.1, 162.8, 165.4, 171.1; IR (KBr) ν 3078, 2950, 1735, 1565, 1442, 1272, 1241, 1129, 743, 701 cm^{-1}; HRMS (FAB) calcd. for $C_{17}H_{15}{}^{79}Br_3{}^{35}Cl_3O_6$: 656.7484 ([M + H]$^+$), found: 656.7485.

3,5-Dibromobenzoate of 2*R*-Chloro-2-hydroxymethyl-4*S*-(2,2,2-trichloroethyl)-2-methoxycarbonylvalerolactone and Its Enantiomer (13). To a mixture of **11** (150 mg, 0.42 mmol), TEA (0.10 mL, 0.72 mmol), and a trace amount of DMAP in DCM (10 mL) was added the freshly prepared acid chloride (1.0 mmol) described above in

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DCM (10 mL) at 0 °C. The mixture was stirred at rt for 12 h. Saturated $NaHCO_3$ aqueous solution was added, and the solution was washed with brine, and then dried over $MgSO_4$. The reaction mixture was concentrated in vacuo, and the residue was recrystallized by hexane/EtOAc to give **13** (205 mg, 79%): mp 169−171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.72 (d, J = 16.0 Hz, 1 H), 3.13 (d, J = 16.0 Hz, 1 H), 3.25 (d, J = 15.4 Hz, 1 H), 3.50 (d, J = 15.4 Hz, 1 H), 3.85 (s, 3 H), 4.61 (d, J = 11.4 Hz, 1 H), 4.70 (d, J = 12.3 Hz, 1 H), 4.88 (d, J = 11.4 Hz, 1 H), 5.20 (d, J = 12.3 Hz, 1 H), 7.89 (t, J = 1.8 Hz, 1 H), 8.04 (d, J = 1.8 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.8, 44.6, 55.4, 58.6, 59.4, 68.0, 69.9, 94.8, 123.3, 131.4, 132.0, 139.1, 162.9, 164.9, 171.1. IR (KBr) ν 3097, 3074, 2954, 1735, 1565, 1442, 1272, 1206, 1129, 701 cm^{-1}; HRMS (FAB) calcd. for $C_{17}H_{15}{}^{79}Br_2{}^{35}Cl_4O_6$: 612.7989 ([M + H]$^+$), found: 612.7979.

4,6-*cis*- and 4,6-*trans*-Bis(methoxycarbonyl)-4-(Phenylmercaptomethyl)-1,1-diisopropyl-1-sila-2,8-dioxacyclooctane (14) and (15). To a mixture of **4** (345 mg, 1.0 mmol) and AIBN (10 mg, 0.06 mmol) in ^{t}BuOH (10 mL) was added thiophenol (220 mg, 2.0 mmol), and the mixture was refluxed for 12 h. After cooling to rt, the solvent was removed in vacuo, and the residue was chromatographed on silica gel (hexane/EtOAc = 10/1) to get a mixture of **14** and **15** (83:17). Further purification was proceeded by chromatography (hexane/EtOAc = 15/1) to afford **14** (276 mg, 61%) and **15** (52 mg, 11%). Analytical pure samples were obtained by preparative HPLC (hexane/THF = 20/1). **14**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97−1.12 (m, 14 H), 2.24 (dd, J = 5.5, 15.6 Hz, 1 H), 2.58 (dd, J = 2.9, 15.6 Hz, 1 H), 2.78 (m, 1 H), 3.11 (d, J = 13.2 Hz, 1 H), 3.27 (d, J = 13.2 Hz, 1 H), 3.49 (s, 3 H), 3.65 (s, 3 H), 3.85−3.90 (m, 2 H), 4.11−4.15 (m, 2 H), 7.16−7.20 (m, 1 H), 7.24−7.28 (m, 2 H), 7.38−7.41 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6, 12.1, 17.2, 17.31, 17.34, 17.36, 31.8, 37.3, 42.1, 51.9, 52.0, 52.3, 65.3, 66.1, 126.5, 128.8, 130.6, 136.1, 173.7. IR (KBr) ν 2947, 2892, 2865, 1743, 1466, 1439, 1248, 1193, 1096, 1065 cm^{-1}; HRMS (FAB) calcd. for $C_{22}H_{35}O_6SSi$: 455.1924 ([M + H]$^+$), found: 455.1924. **15**: ^{1}H NMR (400 MHz, CDCl3) δ 0.97 (m, 1 H), 1.02 (s, 6 H), 1.07 (m, 7 H), 1.86 (dd, J = 6.1, 14.9 Hz, 1 H), 2.47 (dd, J = 2.4, 14.9 Hz, 1 H), 2.69 (m, 1 H), 3.24 (ABq, J = 13.4 Hz, 2 H), 3.47 (s, 3 H), 3.67 (s, 3 H), 3.80 (m, 1 H), 4.03 (m, 1 H), 4.12 (m, 2 H), 7.14−7.18 (m, 1 H), 7.23−7.27 (m, 2 H), 7.40−7.42 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.6, 12.2, 17.33, 17.36, 17.5, 34.7, 39.9, 43.9, 51.7, 52.1, 52.8, 61.8, 66.7, 126.3, 128.8, 130.1, 136.4, 173.0, 173.9. IR (KBr) ν 2951, 2896, 2869, 1735, 1466, 1439, 1264, 1135, 1080, 886 cm^{-1}; HRMS (FAB) calcd. for $C_{22}H_{35}O_6SSi$: 455.1924 ([M + H]$^+$), found: 455.1920.

4,6-*cis*- and 4,6-*trans*-Bis(methoxycarbonyl)-4-[tris-(trimethylsilyl)]silylmethyl-1,1-di-isopropyl-1-sila-2,8-dioxacyclooctane (16) and (17). To a mixture of **4** (400 mg, 1.2 mmol) and AIBN (15 mg, 0.09 mmol) in benzene (15 mL) was added tris(trimethylsilyl)silane (288 mg, 1.4 mmol), and the mixture was refluxed for 12 h. After cooling to rt, the solvent was removed in vacuo, and the residue was chromatographed on silica gel (Hexane/EtOAc = 10/1) to get a mixture of **16** and **17** (75:25). Further purification was proceeded by chromatography (hexane/EtOAc = 15/1) to afford **16** (390 mg, 57%) and **17** (117 mg, 17%). Analytical pure samples were obtained by preparative HPLC (hexane/THF = 20/1). **16**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.16 (s, 27 H), 0.99−1.05 (m, 13 H), 1.09−1.13 (m, 1 H), 1.20 (d, J = 14.5 Hz, 1 H), 1.31 (d, J = 14.5 Hz, 1 H), 2.22 (m, 2 H), 2.87 (m, 1 H), 3.64 (s, 3 H), 3.65 (s, 3 H), 3.66 (d, J = 11.3 Hz, 1 H), 3.91 (m, 1 H), 4.09 (m, 1 H), 4.13 (d, J = 11.3 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 1.3, 11.5, 12.1, 14.1, 17.29, 17.33, 17.37, 17.42, 36.7, 42.9, 50.0, 51.81, 51.83, 65.2, 66.8, 174.0, 175.8. IR (KBr) ν 2951, 2896, 2869, 1739, 1731, 1443, 1244, 1100, 1053, 835 cm^{-1}; HRMS (FAB) calcd. for $C_{25}H_{57}O_6Si_5$: 593.3001 ([M + H]$^+$), found: 593.2989. **17**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.16 (s, 27 H), 1.02−1.05 (m, 14 H), 1.32 (d, J = 14.4 Hz, 1 H), 1.36 (d, J = 14.4 Hz, 1 H), 1.82 (dd, J = 5.9, 14.9 Hz, 1 H), 2.32 (dd, J = 2.6, 14.9 Hz, 1 H), 2.79 (m, 1 H), 3.65 (m, 6 H), 3.70 (d, J = 11.2 Hz, 1 H), 3.76 (dd, J = 10.6, 11.1 Hz, 1 H), 4.07 (dd, J = 3.4, 11.1 Hz, 1 H), 4.11 (d, J = 11.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 1.4, 11.8, 12.1, 17.3, 17.42, 17.46, 17.5, 38.9, 44.6, 50.6, 51.7, 51.9, 66.1, 66.9, 174.2, 175.3. IR (KBr) ν 2951, 2896, 2869, 1743, 1727, 1303, 1244, 1131, 1069, 835 cm^{-1}; HRMS (FAB) calcd. for $C_{25}H_{57}O_6Si_5$: 593.3001 ([M + H]$^+$), found: 593.2996.

4,6-*cis*- and 4,6-*trans*-Bis(methoxycarbonyl)-4-(phenylmercaptomethyl)-1,1-di-methyl-1-sila-2,8-dioxacyclooctanes (18) and (19). To a mixture of **5** (400 mg, 1.4 mmol) and AIBN (20 mg, 0.12 mmol) in ^{t}BuOH (15 mL) was added thiophenol (300 mg, 2.7 mmol), and the mixture was refluxed for 12 h. After cooling to rt, the solvent was removed in vacuo to give a mixture of **18** and **19** in addition to other unidentified products. The ratio of **18** and **19** was estimated to be 60% and 40% based on the integration of the peaks of the NMR spectrum of the crude mixture at δ 2.20 (dd, 1 H for **18**, relative integration = 1.00) and δ 2.83 (m, 1 H for both **18** and **19**, relative integration = 1.65). Attempts to purify **18** and/or **19** by column chromatography on silica gel were unsuccessful, **18** and **19** being decomposed under these conditions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of new compounds and/or 2D ROESY of **14**−**17**, Cartesian coordinates of **20** by DFT calculation, and crystal data of **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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